PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Olufunmilayo I. Olopade

Serial No.: 08/674,311

Filed: July 1, 1996

For: METHYLTHIOADENOSINE PHOSPHORYLASE COMPOSITIONS AND METHODS OF USE IN THE DIAGNOSIS AND TREATMENT OF PROLIFERATIVE DISORDERS

Group Art Unit: 1655

Examiner: L. Arthur

Atty. Dkt. No.: ARSB:509—1

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37 C.F.R. § 1.8

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June 7, 2002
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Thomas M. Boyce

APPEAL BRIEF

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BOX AF
Commissioner of Patents
Washington, D.C. 20231

Sir:

Appellant hereby submits an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences in response to the Final Official Action mailed July 5, 2001. The Notice of Appeal was mailed on November 5, 2001 with an appropriate certificate of mailing. The Notice was received by the Patent and Trademark Office on January 8, 2002. Thus, the Appeal Brief was due on March 8, 2002. The enclosed petition for an extension of time of three months with accompanying fee payment brings the due date to June 8, 2002.

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The fee for filing this Appeal Brief is $160.00 and is attached hereto. Should any fee be deficient or absent, please consider this paragraph a request and authorization to withdraw the appropriate fee. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed material, or should an overpayment be included herein, the Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski L.L.P. Account No.: 50-1212/10008123/TMB.

PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136(a), Appellant petitions for an extension of time of three months, to and including June 8, 2002, in which to file an Appeal Brief due March 8, 2002. Pursuant to 37 C.F.R. § 1.17, a check in the amount of $460.00 is enclosed, which is the process fee for a three-month extension of time for a small entity. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski Deposit Account No. 50-1212/10008123/TMB.

I. REAL PARTY IN INTEREST

The real party in interest is the assignee, Arch Development Corporation, 1101 East 58th Street, Chicago, Illinois.

II. RELATED APPEALS AND INTERFERENCES

There are no interferences or appeals for related cases.

III. STATUS OF THE CLAIMS

Claims 1-38 were originally filed in the present application.

Claims 1-38 have been cancelled. Claims 39-96 were added by preliminary amendment filed concurrently with the request for continued prosecution under 37 C.F.R. §1.53(d) filed August 19, 1999. Claims 54, 57, 67, 68, 70 and 71 were amended and claims 95 and 96 were cancelled by an amendment filed April 12, 2001. Claims 39-94 were therefore pending at the time of the Final Office Action mailed July 5, 2001. In the Final Office Action claims 39-94 were rejected. Claims 39-94 are the subject of this appeal. A summary of the claims under appeal, in what Appellants believe is their correct status if the amendment is not entered is submitted in Appendix A of this brief. A summary of the claims under appeal, in what Appellants believe is their correct status if the amendment is entered is submitted in Appendix B of this brief.

Appellants have submitted an Amendment concurrent with this Appeal Brief. This Amendment places the claims in better condition for appeal by correcting the dependency of claim 91 to depend from claim 90 instead of claim 88. The amendment also corrects a typographical error in the preliminary amendment of August 19, 1999, which incorrectly recited a filing date of July 2, 1995 for application serial number 60/000,831 of which the present application claims the benefit of priority. The correct filing date of application serial number 60/000,831 is July 3, 1995.

IV. STATUS OF AMENDMENTS

An amendment under 37 C.F.R. 1.116 has been filed concurrently with this Appeal Brief. No other amendments are pending. A summary of the claims under appeal, in what Appellants believe is their correct status if the amendment is not entered is submitted in Appendix A of this brief. A summary of the claims under appeal, in what Appellants believe is their correct status if the amendment is entered is submitted in Appendix B of this brief.

V. SUMMARY OF THE INVENTION

This invention describes novel nucleic acid and peptide compositions comprising methylthioadenosine phosphorylase (MTAP) and methods of use for MTAP polypeptides and nucleic acids encoding such peptides in the detection of MTAP nucleic acids, diagnosis of proliferative disorders, and the making of MTAP polypeptides and related compositions.

VI. ISSUES ON APPEAL

The issues for the Board's consideration are:

(A) Whether Kamb *et al.* (1994) anticipates the present invention ;

(B) Whether Nobori *et al.* (1994) anticipates the present invention; and

(C) Whether the present invention is obvious in view of Nobori *et al.* (1994).

VII. GROUPING OF THE CLAIMS

For purposes of this Appeal, the claims do not stand or fall together as set forth in the Argument below.

With respect to the separate patentability of the claims, proper rejection under 35 U.S.C. §102 requires that the cited art disclose each and every limitation of the rejected claims. Further, proper rejection under 35 U.S.C. §103(a) requires that the Examiner establish that the elements missing from a broader claim but present in a narrower claim are taught in the art. Appellant has seen nothing in the record to suggest that the Examiner has met this burden with regard to each and every limitation of each of the claims. Therefore, even if the broadest claims were found to be anticipated or obvious, which they are not, the balance of the claims, on the basis of the record, would not be. Therefore, the claims should stand or fall separately.

Grounds and argument for separate patentability of the claims are presented in the arguments against rejection provided below (Section VIII). Additional grounds for separate patentability are also provided therein (Section VIII G).

VIII. ARGUMENT

A. Rejections under 35 U.S.C. §102(b): The Legal Standard for Anticipation

Anticipation requires that "the four corners of a single, prior art document describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation" *Advanced Display Systems Inc. v. Kent State University,* 212 F.3d 1272, 1282, 54 USPQ2d 1673, 1679 (Fed. Cir. 2000), cert. Denied, 121 S. Ct. 1226 (2000), citing *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999) and *In re Paulsen*, 30 F.3d 1475, 1479, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994). If the reference expressly lacks a claimed element, the reference may yet anticipate via inherency if it makes "clear that the missing descriptive matter is ***necessarily*** present in the thing described in the reference, and that it would be so recognized

by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, (Fed. Cir. 1991), emphasis added.

B. The invention is not anticipated by Kamb *et al.* (1994).

The Final Office Action (Appendix E) rejects claims 39-50, 52, 53, 59, 67-76, 78, 80-83, 88-94 under 35 U.S.C. §102(b) as being anticipated by Kamb *et al.* (1994) *Science* 264:436-440 (Appendix C). Appellant respectfully traverses the rejection.

1. Kamb *et al.* does not disclose a single one, let alone all, of the elements as claimed.

Appellant can find no description of any elements of the rejected claims, whether graphic or verbal in the entirety of the Kamb *et al.* reference (Appendix C). The present claims are to isolated nucleotides comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 (the MTAP protein), portions of SEQ ID NO: 2, and isolated nucleotides identical or complementary to at least 21 contiguous nucleotides of SEQ ID NO: 1. The claims thus require that an anticipating reference disclose nucleotide sequences that encode at least a portion of the MTAP amino acid sequence. Yet, no such sequences can be found in the Kamb *et al.* reference.

Appellants respectfully submit in support of this appeal the Declaration of Prof. Janet D. Rowley, M.D., D.Sc. (Appendix I). Prof. Rowley's Declaration states that Kamb et al. (1994) do not present any sequence data other than those of the MTS1 and MTS2 loci, which do not indicate that a gene encoding MTAP exists in their clones. Paragraph 6 of the Rowley Declaration (Appendix I). Further, "No other data are provided that might suggest that the gene

for MTAP lines in the cloned region. In fact, Kamb et al. (1994) never discuss whether the MTAP gene lies in the region at all." Paragraph 7 of the Rowley Declaration (Appendix I).

In accord with the Declaration of Prof. Rowley, no mention of MTAP, nor any allusion to its existence is to be found in the entire text of Kamb *et al.* and the rejection does not identify in the Kamb *et al.* reference where the elements of the claims may be found. Kamb *et al.* therefore does not expressly anticipate the present claims.

2. Kamb *et al.* cannot support an argument of anticipation via inherent properties.

Although never expressed as such, viewed in the most generous light the Examiner's arguments for rejection appear to express an argument for anticipation via the inherent properties of what is disclosed by Kamb *et al.* But for a reference to so anticipate, it "must make clear that the missing descriptive matter is ***necessarily*** present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, (Fed. Cir. 1991). (Emphasis added.) Such is not the case here.

The complete Examiner's argument for anticipation is that "The cosmid that contains MTS1 of Kamb *et al.* also contains the human methylthioadenosine phosphylase gene (MTAP) since these two genes are tightly linked." The Final Action, page 2, lines 14-15. Exactly which of the eleven cosmids disclosed in Kamb *et al.* is thought to contain MTAP is not actually identified but for the reference to cosmid "C5" found in the Examiner's response to Appellant's arguments. See the Final Action, page 4, lines 4-5. Additionally, exactly which of the two loci, MTS1 or MTS2 is intended to be the gene "tightly linked" to MTAP is also not indicated. Appellant further notes that the argument does not define nor reference what constitutes

sufficiently "tight linkage." In any case, however, Appellant respectfully submits that the argument for inherent anticipation is factually incorrect and legally insufficient.

The Examiner asserts that "tight linkage" between two genes is sufficient to render ***certain*** that any cosmid clone containing one gene will ***necessarily*** contain at least a portion of the other. But this is demonstrably not the case. Indeed, the Kamb *et al.* reference itself provides sufficient examples to invalidate the Examiner's argument. For example, cosmid c67 of the Kamb *et al.* reference contains the MTS1 gene, but does not contain the MTS2 gene. Fig. 1.A. of Kamb *et al.*, page 437. Similarly, the c12 cosmid contains MTS2 but not MTS1. Yet, undeniably, the MTS1 gene is within 40 kb of MTS2 (by the scale provided in the figure). MTS1 and MTS2 are therefore presumably "tightly linked." Under the reasoning of the rejection, any cosmid containing the MTS1 gene would necessarily contain the MTS2 gene. Yet, this is factually not the case.

This simple example, culled from the very reference upon which the rejection is based makes clear why the Kamb *et al.* reference cannot anticipate the present invention. A cosmid clone containing one gene does not necessarily contain a second gene unless there is independent evidence that it does -- even if the genes are so "tightly linked" as to be within the length of a cosmid (about 40,000 bp) of each other. The scientific basis for this fact, as appreciated by those of skill in the art at the time of filing, is that what a clone of any size contains is a function of the location of its boundaries, and not the genetic or physical distance between loci.

Appellants refer to the Declaration of Prof. Rawley, Appendix I, which states "Kamb et al. (1994) also do not provide any other data suggesting that the cloned region contains a gene for MTAP. Such data could include the presence of genetic markers further distal or proximal to

MTS1 and MTS2 that are known to bound the region containing the MTAP gene. However, Kamb et al. (1994) do not show or discuss such markers. The markers used are not known to bound the region containing the MTAP gene." Paragraph 7 of the Rawley Declaration (Appendix I). Therefore, the boundaries of the clones provided in Kamb *et al.* are not disclosed to overlap or even come close to the sequences encoding MTAP. Thus, the skilled artisan at the time of publication of Kamb *et al.* and the filing of the present application, would not view the clones disclosed by Kamb *et al.* as necessarily containing the sequences encoding MTAP, *i.e.* the sequences of the present invention. "Based upon my skill and training in the area of molecular biology and genetics, I can say that there is no evidence whatsoever in the Kamb et al. (1994) paper that would lead one to conclude that the gene for MTAP is contained in any of the clones Kamb et al. made." Paragraph 9 of the Rawley Declaration (Appendix I).

Indeed, the disclosure of the Appellant's specification itself refutes the specific inherency argument advanced to support rejection of the claims. Analysis of the entire region that does separate the MTS1 and MTS2 genes from the MTAP gene confirms what the Appellant, and others of skill in the art at the time supposed to be the case – that the MTAP gene sequence lies 80,000 base pairs further towards the telomere of Chromosome 9. FIG. 1. and pages 49-56 of the Specification. Also see paragraph 4 of the Rawley Declaration (Appendix I), and Gursky et al. (2002) (Appendix J). Appellant notes that this distance is beyond the scale of the Kamb *et al.* Fig. 1 and beyond the reach of any of the clones disclosed by Kamb *et al.*

In sum, the Kamb *et al.* reference cannot expressly anticipate the present invention and the implied argument that the Kamb *et al.* disclosure inherently anticipates the present invention is logically and factually incorrect. Since it was not, indeed could not, be scientifically certain

that the cosmid c5, or any of the clones disclosed by Kamb *et al.* contains any sequence encoding MTAP, the disclosure of Kamb *et al.* cannot anticipate the present claims.

Appellant respectfully requests that the rejection be overturned.

C. The invention is not anticipated by Nobori *et al.* (1994).

The Final Office Action rejects claims 54-66, 74-76, 78-83, and 88-94 under 35 U.S.C. §102(b) as being anticipated by Nobori *et al.* (1994) Nature 368:753-756. Appellant respectfully traverses the rejection.

1. Nobori *et al.* does not disclose all of the elements of the claims.

Appellant can find no description of the entirety of the elements of the rejected claims, whether graphic or verbal in the entirety of the Nobori *et al.* reference. The present claims are to isolated nucleotides comprising a sequence region identical or complementary to at least 21 contiguous nucleotides of SEQ ID NO: 1, or to isolated nucleotides of a sequence that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 (the MTAP protein), or portions of SEQ ID NO: 2. The claims thus require that an anticipating reference disclose the nucleotide sequences that encode at least a portion of the MTAP amino acid sequence as well as the MTAP amino acid sequence itself. These sequences are specific limitations of the claims. Yet, no such sequences can be found in the Nobori *et al.* reference. Neither nucleotide sequences nor amino acid sequences of MTAP are listed in the text, figures, or footnotes of the Nobori *et al.* reference. Appellant respectfully submits that Nobori *et al.* therefore does not expressly anticipate the present claims.

2. Nobori *et al.* cannot anticipate because it does not describe nor enable the present invention.

Despite the lack of express anticipation, the claims are rejected because the text of Nobori *et al.* states that "MTAP cDNA was isolated and used to probe a human placenta lambda-phage library. A 2-kilobase (kb) HindIII fragment (clone 7-2) contained the 3' end of the MTAP gene by sequence analysis." Nobori *et al.* page 753, second paragraph of text. This statement, (and its paraphrase, found in the legend to FIG. 1 b, page 754 of Nobori *et al.*) is the sum total of disclosure provided by the Nobori *et al.* reference that is relevant to the cloning and sequencing of the MTAP gene and determination of the amino acid sequence of human MTAP.

Appellant notes that the legal standard for anticipation requires that "the four corners of" Nobori *et al.* "describe every element of the claimed invention, either expressly or inherently, such that a person of ordinary skill in the art could practice the invention without undue experimentation" *Advanced Display Systems* at 1282. The disclosure of Nobori *et al.* does not meet this standard because the sole allusion to the presently claimed invention provided by Nobori *et al.* is found in the tantalizingly opaque statements that "MTAP cDNA was isolated..." and that "(clone 7-2) contained the 3' end of the MTAP gene by sequence analysis." No specific sequence of the *MTAP* gene nor means by which one of skill in the art could obtain the MTAP cDNA is provided by Nobori *et al.*

However, in order to practice the present invention one of skill would have to first obtain an MTAP cDNA, its sequence, and verify that it encoded the MTAP polypeptides of the present claims. Appellant respectfully points out that to do so would require an undue amount of experimentation, since no specific guidance is provided by Nobori *et al.* as to how the "MTAP cDNA was isolated...." Appellant respectfully submits that a mere allusion to what might be

part of the invention is not sufficient to enable the artisan to practice the present invention, and so place it in the hands of the public.

It is well established law that to satisfy 35 U.S.C. §102(b) a printed publication must describe the invention so as to place it in the hands of the public and the artisan. *In re Wiggins*, 488 F.2d 538, 543, 179 USPQ2d 421, 424-25 (C.C.P.A. 1973). In this light, merely naming a complex chemical compound, without providing a means to obtaining it, does not anticipate the compound. *Id.* Therefore, in order to anticipate, the Nobori *et al.* reference must at least sufficiently describe the elements of the present invention as well as how to make it. *In re Wiggins*, at 543; *In re Hoeksema*, 399 F.2d 269, 273, 158 USPQ 596, 600 (C.C.P.A. 1962). With specific reference to nucleotide sequences encoding genes, the definition of a gene requires disclosure of its sequence so that it may be distinguished from others, as well as how to make it. *Amgen, Inc. v. Chugai Pharmaceutical Company, Ltd.*, 927 F.2d 1200 (Fed. Cir. 1991). The disclosure of the Nobori *et al.* reference does not satisfy this standard.

Appellant respectfully submits that the entirety of the Nobori *et al.* reference is devoid of any description whatsoever of any part of the gene encoding MTAP. Nobori *et al.* is also devoid of any description of how to obtain the *MTAP* gene. The mere recitation that "MTAP cDNA was isolated..." and that a clone "contained the 3' end of the MTAP gene" does not sufficiently describe the present invention because it provides no sequence data whatsoever. The mere recitation of the words "MTAP cDNA" does not sufficiently describe the nucleotide sequence. *EnzoBiochem, Inc., v. Gen-Probe Inc.*, 01-1230 (Fed. Cir., April 2, 2002) (Fed. Cir. BBS). The bare statement that a "MTAP cDNA was isolated" does not tell how to make it. *Wiggins* at 543.

Appellant respectfully submits, that although the language of Nobori *et al.* might be tantalizingly similar to that which would typically accompany the full (or even partial) disclosure of a gene sequence, it does not provide any description of the sequence of the *MTAP* gene whatsoever, and therefore does not provide its full (or even partial) definition. Additionally, Nobori *et al.* provides no means whatsoever for obtaining it. Nobori *et al.* therefore does not describe the present invention and therefore cannot anticipate the present claims. Appellant respectfully submits that the rejections be withdrawn.

D. Rejections under 35 U.S.C. §103(a): The Legal Standard of Obviousness

In reviewing these rejections, the Board should bear in mind the high standard by which an obviousness rejection is judged. The Federal Circuit, in the case of *In re Vaeck,* 20 USPQ 2d 1438 (Fed. Cir. 1991), stated that an Examiner must establish two criteria in order to make a *prima facie* case of obviousness:

1) the prior art would have suggested to one of ordinary skill in the art to make the composition as claimed; and

2) the prior art demonstrates a reasonable expectation of success of the invention.

Vaeck also emphasizes that both the suggestion and reasonable expectation of success must be found in the prior art, not in the Appellant's disclosure. Furthermore, "[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson,* 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). And, *all* of the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974).

The burden of showing a *prima facie* case of obviousness is on the Examiner, who must show evidence beyond merely stating that the claimed invention is obvious in light of the prior

art. *See Manual of Patent Examining Procedure* 2144.03; *Graham v. John Deere Co.*, 383 U.S. 1, 18 (1966). Appellant respectfully notes that here the present rejection is in view of a single reference, Nobori *et al.* (1994), but that if more than this reference is relied upon in constructing a case of obviousness, a motive to combine the elements disclosed by the several references must be found in the prior art or knowledge of the ordinary artisan. *In re Mills*, 916 F.2d 680, 682 (Fed. Cir. 1990).

Lastly, if the Examiner properly meets the burden of showing a *prima facie* case of obviousness, the Appellant may still overcome the rejection through a showing of secondary considerations such as unexpected results, long felt need, failure by others or commercial success. *See Id.* at 17-18.

E. The invention is not obvious in view of Nobori *et al.* (1994)

The Final Office Action rejects claims 39-42, 45-66, 74, 75, 77-83, and 88-94 under 35 U.S.C. § 103(a) as obvious over Nobori *et al.* (1994) (Appendix D), referencing the grounds for rejection asserted in the Office Action of February 8, 2000 (Appendix G). See page 6, lines 18-19 of the Final Office Action (Appendix E) and page 7, lines 3-4 of the Action of October 12, 2000 (Appendix F).

The Action of February 8, 2000 asserts that Nobori *et al.* "disclose a highly specific probe for isolating the complete coding sequence for the MTAP gene" and that the use of the disclosed probe in obtaining the MTAP gene would be routine, motivated by the desirability of having the complete cDNA and a desire to obtain large quantities of recombinant MTAP. The Action of February 8, 2000, page 4 through page 5, line 6 (Appendix G).

Appellant respectfully points out that, as explained above, the Nobori *et al.* reference does not contain all the limitations of the claims, does not disclose any portion of a "highly specific probe" for MTAP, does not enable what it does disclose, and therefore provides no reasonable expectation of success in making the present invention. Appellant therefore respectfully traverses the rejection.

1. All Claim Limitations Must be Taught or Suggested by Prior Art.

The holding in *In re Royka*, 490 F.2d 981 (CCPA 1974) states that *all* of the claim limitations must be taught or suggested by the prior art. Here, in order for the Nobori *et al.* reference to form the basis of a rejection under 35 U.S.C. §103(a), it must disclose or suggest, not only polynucleotides encoding portions of human MTAP, but also, *inter alia*: polypeptides comprising the amino acid sequence of SEQ ID NO: 2 (*i.e.* the entire amino acid sequence of human MTAP) or subsequences thereof; polynucleotides encoding SEQ ID NO: 2 operably positioned under the control of promoters; such polynucleotides operatively linked to a second sequence encoding a fusion polypeptide; polynucleotide constructs in cells; methods of detecting MTAP encoding polynucleotides, including methods within intact cells, *etc.*

As presented below, in specific argument regarding the separate patentability of the claims, Appellant has seen nothing in the record to suggest that the Examiner has met this burden with regard to all the claim limitations of all the rejected claims. Indeed, "[t]here is no argument that Nobori *et al.* Does [sic] not teach the complete MTAP gene of SEQ ID NO: 1 encoding the a [sic] polypeptide of SEQ ID NO: 2." The Final Office Action, page 7, lines 12-13 (Appendix E). But Appellant respectfully points out that the Nobori *et al.* text does not operably disclose ***any*** *MTAP* gene sequence, nor ***any*** MTAP polypeptide sequence, and as presented below, does not

provide the artisan with any reasonable expectation of success in acquiring these sequences nor practicing the present invention.

2. The Disclosure of Nobori *et al.* is Not Enabled and is Not Enabling.

Appellant respectfully reiterates the arguments presented above in response to the rejections under 35 U.S.C. §102(b) grounded on the disclosure of Nobori *et al.* In brief, the text of Nobori *et al.*, although reciting the words "MTAP cDNA" and naming a clone allegedly containing a portion of the MTAP coding sequence, contains no sequence data or other means by which one of skill in the art could possibly recognize or obtain such a cDNA (or any other claimed elements) in order to practice the present invention.

3. Nobori *et al.* provides no reasonable expectation of success in making or practicing the present invention.

The argument for rejection asserts that Nobori *et al.* disclose "a highly specific probe for isolating the complete coding sequence for the MTAP gene." The Office Action of February 8, 2000. Appellant respectfully submits that Nobori *et al.* does not disclose sufficient information to allow the inference that whatever Nobori *et al.* does disclose is in any way "highly specific," authentic, or enables the ordinary artisan to make and practice the present invention.

The argument advanced in support of the obviousness rejection relies upon an alleged specificity of a clone discussed in Nobori *et al.* for the human MTAP encoding sequence. But as is appreciated by those of skill in the art, specificity of probe is largely a function of sequence similarity and Nobori *et al.* do not disclose either their candidate sequence, nor any other that may be used to evaluate the alleged property of specificity, let alone authenticity of the probe. Nobori *et al.* simply does not provide data that allows the artisan to compare a nucleotide

sequence of their candidate clone with any known nucleotide or amino acid sequence known to be even remotely similar to human MTAP.

In fact, the physical location of the clone named by Nobori *et al.* (1994) does not overlap that of clones containing the authentic MTAP gene. As admitted by the subsequence publication of Nobori *et al.* (1996) (Appendix H), the map of Nobori *et al.* (1994) (Appendix D) places the cloned fragments in an incorrect order, and so incorrectly identifies the locations of the putative gene sequences. The only gene sequence data disclosed by Nobori *et al.* (1994) is that of the CDK4-inhibitor gene (FIG. 2, page 755, Appendix D) Thus, based upon the disclosure of Nobori *et al.* , the ordinary artisan would at most be able to initiate a chromosome walk from CDK4 inhibitor gene towards the putative MTAP locus. However, Nobori *et al.* would direct the artisan in exactly the wrong direction in which to walk.

The argument in rejection asserts that such a walk is not the only means by which an ordinary artisan would be able to clone the authentic *MTAP* gene. However, Appellant respectfully notes that the Nobori *et al.* (1994) reference does not disclose or otherwise provide the artisan with any portion of the MTAP gene and therefore does not enable the approach referred to by the argument in rejection, *i.e.* the screening of a cDNA library.

This vacuum of information outlined by Nobori *et al.* (1994) can in no way form the basis for an ordinary artisan's reasonable expectation of success in cloning of the complete and authentic MTAP encoding sequence. Rather, one would have to follow the disclosure and methods of the present application. But using the Appellant's disclosure as a source of guidance to find the claimed invention obvious is never proper. *W. L. Gore v. Garlock, Inc.,* 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983); *In re Dembiczak,* 175 F.3d 994, 999, 50

USPQ2d 1614, 1617 (Fed. Cir. 1999). Given the absence from Nobori *et al.* of the necessary information required for the ordinary artisan to make and practice the present invention, Appellant respectfully submits that that no reasonable expectation of success can be garnered from the disclosure of Nobori *et al.* in view of the knowledge and skill of the ordinary artisan at the time the application was filed.

4. At best, Nobori *et al.* may make it obvious to try to make the present invention.

The argument in rejection contends that Nobori *et al.* (1994) discloses a highly specific probe for isolating the complete coding sequence for the *MTAP* gene, and that the ordinary artisan would be highly motivated to obtain the remainder of the *MTAP* gene. But the argument mistakenly assumes that a clone allegedly containing a small, unspecified portion of a gene, and used as a probe to initiate a chromosome walk would motivate one of skill to search for the entire gene. The Patent Office appears to assert it has more knowledge than the skilled artisans and thus, it is substituting its judgment for that of an established expert in the art. This is improper. *In re Zeidler*, 682 F.2d.961, 966-967 (Fed. Cir. 1982).

At best, the argument proposes a fishing expedition for those of skill in the art. In view of Nobori *et al.* (1994), one skilled in the art might find it ***obvious to try*** to obtain the sequence of the gene encoding human MTAP. But this is not the standard of 35 U.S.C. § 103. *In re Geiger,* 815 F.2d 686 (Fed. Cir. 1987). "'Obvious to try' has long been held not to constitute obviousness." *In re Deuel,* 51 F.3d 1552 (Fed. Cir. 1995) (citing *In re O'Farrell,* 853 F.2d 894 (Fed. Cir. 1988)). An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result

or indicate that the claimed result would be obtained if certain directions were pursued. *In re Eli Lilly & Co.*, 902 F.2d 943 (Fed. Cir. 1990). Here, the disclosure of Nobori *et al.* does not contain sufficient teaching of how to obtain the specific sequence of the gene encoding authentic human MTAP. A particular result, such as the sequence of a nucleotide comprising a gene for MTAP, is not made obvious by a general incentive, nor by the existence of techniques by which those efforts can be carried out. *In re Deuel,* 51 F.3d at 1559. "The fact that one can conceive a general process in advance for preparing an undefined compound does not mean that a claimed specific compound was precisely envisioned and therefore obvious." *Id.*

Appellant reiterates that a precise vision of any part of the gene encoding MTAP requires its sequence. With reference to gene sequences, "...conception has not been achieved until reduction to practice has occurred, *i.e.* until after the gene has been isolated." *Amgen, Inc. v. Chugai Pharmaceutical Company, Ltd.,* 927 Fed. 2d at 1206. Nobori *et al.* does not identify the structure or physical characteristics of the *MTAP* gene. Additionally, Appellant respectfully notes that the existence of a general method of isolating DNA molecules is essentially irrelevant to the question whether the specific molecules themselves would have been obvious. *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993).

Since the Nobori *et al.* reference does not disclose all the limitations of the claimed invention, does not enable what it does disclose relevant to the invention, and does not provide any basis for a reasonable expectation of success in making and practicing the present invention, Appellant respectfully submits that the rejection is improper. Appellant respectfully requests that the rejection be overturned.

5. Claims 84-87 are not obvious, and separately patentable.

Claim 84 and its dependents are separately rejected as obvious in view of Nobori *et al.* The Final Office Action, page 8, lines 10-11. Claims 84-87 recite detection kits comprising, in suitable container means, a first nucleic acid segment comprising at least 21 contiguous nucleotides of SEQ ID NO:1 and a detection reagent. The argument for rejection asserts that Nobori *et al.* discloses the association of the 9p21-22 region with cancer and that this region was suspected of containing a number of tumor suppressor genes. Office Action of February 8, 2000, page 6, line 1-3. The argument further alleges "[t]herefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have packaged the polynucleotides and vectors taught by Nobori et al Or Bolander *et al.* With [sic] detection reagents in a kit in order to achieve the expected benefit of providing probes to use in a method of screening for deletions of the 9p21-22 region as suggested by Nobori *et al.* And by Bolander *et al.* In a convenient form which was easier to distribute and market." Office Action of February 8, 2000, page 6, lines 4-9. Appellant traverses.

First, Appellant notes that the rejection based upon the Bolander *et al.* reference has been withdrawn since the Final Office Action withdrew any rejections which had not been reiterated (Final Office Action page 2, line 3) and the present rejection is asserted solely in view of Nobori *et al.* (1994). Final Office Action page 6, lines 18-19.

Nevertheless, as argued above, Nobori *et al.* does not enable the artisan to make or practice any embodiment of the present invention. But with respect to the present rejection, the limitations of the claims are drawn to a detection kit nowhere to be found in any of the cited references. As discussed above, all claim limitations must be found in the cited art. Appellant

has seen nothing in the record that supports the rejection of claims 84-87 as obvious over Nobori *et al.* The limitations to kit components are not addressed at all by the arguments advanced in rejection.

If the Examiner is not convinced of the non-obviousness and independent patentability of claims 84-87, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claims, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

Furthermore, mere conclusory statements that a kit is obvious in view of Nobori *et al.* is not sufficient to establish either that the elements of the invention are present or that the artisan would be specifically motivated to combine those elements. The factual question of motivation is material to patentability, and cannot "be resolved on subjective belief and unknown authority." *In re Lee,* 277 F.3d 1338, 1343 (Fed. Cir. 2002). The argument for rejection of claims 84-87 cites no authority disclosing the limitations of the claims. But even if those elements were to be found, the argument provides no specific motivation to combine beyond subjective belief. Appellant therefore respectfully submits that the kits of claims 84-87 cannot be found obvious in view of Nobori *et al.* Appellant therefore respectfully requests that the rejection be overturned. Appellant also respectfully notes that claims 84-87 are therefore separately patentable over the balance of the claims.

F. If an Independent Claim is Novel and Not Obvious, all of its Dependent Claims Are Novel and Not Obvious.

Once the rejections of the independent claims for anticipation and obviousness have been overcome, similar rejections of claims depending therefrom are also overcome. As set forth in *In re Fine*, 837 F.2d 1071, 1076 (Fed. Cir. 1988), establishing the non-obviousness of an independent claim necessarily establishes the non-obviousness of claims depending therefrom.

G. Separate Patentability.

Appellant respectfully submits that each claim is separately patentable and therefore stands or falls separately as set forth in the arguments above and in Section VII. Appellant here provides additional grounds for separate patentability of the claims.

1. Claim 39 and its dependents are not anticipated, not obvious, and separately patentable from the balance of the claims.

Claim 39 recites an isolated nucleotide comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Claim 39 therefore contains the express limitation that the nucleotide sequence encodes a polypeptide that itself comprises the amino acid sequence of SEQ ID NO: 2. SEQ ID NO: 2 provides the entire amino acid sequence of human MTAP. As argued above, claim 39 is neither anticipated by the Kamb *et al.* reference nor rendered obvious by the Nobori *et al.* reference. Furthermore, the limitations of claim 39 include at the least the limitation that the polypeptide comprise the amino acid sequence of SEQ ID NO: 2, which confers a scope separate from the remaining claims. Thus, even if a claim to a nucleotide encoding a polypeptide comprising less than the amino acid sequence of SEQ ID NO: 2 were to be held unpatentable, which in any event Appellant argues would not be

proper, claim 39 would remain patentable. Claim 39 and its dependents are therefore separately patentable.

2. Claims 40-53 are also novel, not obvious, and separately patentable.

As explained in above, a rejection to dependent claims 40-53 is overcome once an rejection to independent claim 39 is overcome. Therefore, dependent claims 40-42 and 45-53 are not obvious over Nobori *et al.* and claims 40-50, 52 and 53 are not anticipated by Kamb *et al.* for the reasons advanced above. Since they each recite additional limitations, each of which confers patentable novelty and each of which is not obvious over the cited art, dependent claims 40-53 are each separately patentable from the balance of the claims.

(a) Claims 43 and 44 are each separately patentable.

Claims 43 and 44 recite an isolated nucleotide wherein said sequence region comprises the sequence from nucleotide 122 to nucleotide 970 of SEQ ID NO:1 and the sequence of SEQ ID NO:1, respectively. Claims 43 and 44 are rejected solely as anticipated by Kamb *et al.* Since these claims are not anticipated, as argued above, and they are free of any other rejection, they are separately patentable from the balance of the claims.

(b) Claim 45 is separately patentable.

Claim 45 recites an isolated nucleotide comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide promotes melanoma senescence. Appellant has seen nothing in the record that supports the rejection of claim 45 as obvious over Nobori *et al.* or anticipated by Kamb *et al.*. The limitation

wherein the polypeptide promotes melanoma senescence is not found in Nobori *et al.*, nor Kamb *et al.*, and is not addressed at all by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 45, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

(c) Claim 46 is separately patentable.

Claim 46 recites an isolated nucleotide comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide suppresses glioma cell tumor generation. Appellant has seen nothing in the record that supports the rejection of claim 46 as obvious over Nobori *et al.* or anticipated by Kamb *et al.*. The limitation wherein the polypeptide promotes melanoma senescence is not found in Nobori et al, nor Kamb *et al.*, and is not addressed at all by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 46, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

(d) Claim 51 is separately patentable.

Claim 51 is rejected solely as obvious in view of Nobori *et al.* However, claim 51 recited the isolated nucleotide of claim 39, wherein said coding region is operatively linked to a second coding region that encodes a selected peptide or polypeptides, said nucleotide encoding a MTAP fusion peptide or polypeptide. Appellant has seen nothing in the record that supports the rejection of claim 51 as obvious over Nobori *et al.* The limitations of the claim, at least the limitation requiring a MTAP fusion peptide or polypeptide, are not found in Nobori et al, and are not addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 51, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

(e) Claim 52 is separately patentable.

Claim 52 recites an isolated nucleotide comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, wherein the nucleotide is comprised within a vector. Appellant has seen nothing in the record that supports the rejection of claim 52 as obvious over Nobori *et al.* or anticipated by Kamb *et al.*. Appellants note that the limitations of the claims specify that the nucleotide sequence region encode at least the amino acid sequence of SEQ ID NO: 2. No such sequence region is disclosed or suggested by Nobori *et al.* or Kamb *et al.* and therefore its presence in a vector is similarly not obvious or anticipated.

If the Examiner is not convinced of the independent patentability of claim 52, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

(f) Claim 53 is separately patentable.

Claim 53 recites an isolated nucleotide comprising a sequence region that encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, wherein the nucleotide is comprised within a host cell. Appellant has seen nothing in the record that supports the rejection of claim 53 as obvious over Nobori *et al.* or anticipated by Kamb *et al.*. Appellants note that the limitations of the claims specify that the nucleotide sequence region encode at least the amino acid sequence of SEQ ID NO: 2. No such sequence region is disclosed or suggested by Nobori *et al.* or Kamb *et al.* and therefore its presence in a cell is similarly not obvious or anticipated.

If the Examiner is not convinced of the independent patentability of claim 52, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

3. Claim 57 is separately patentable.

Claim 57 recites a nucleotide sequence encoding an MTAP polypeptide, wherein the nucleotide sequence is operably linked to a heterologous promoter. Appellant has seen nothing in

the record that supports the rejection of claim 57 as either anticipated or obvious over Nobori *et al.* The limitations of the claim are not present in the reference and not addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 57, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

4. Claim 58 is separately patentable.

Claim 58 recites a nucleotide sequence encoding an MTAP polypeptide, wherein the nucleotide sequence is operably linked to a heterologous promoter selected from the group consisting of a RSV, CMV, LTR, Sv40, *lac*, *trp*, *tac*, lacUV5, and a T7 promoter. Appellant has seen nothing in the record that supports the rejection of claim 58 as either anticipated or obvious over Nobori *et al.* The limitations of the claim are not present in the reference and not specifically addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 58, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

5. Claim 59 is separately patentable.

Claim 59 recites a nucleotide sequence encoding an MTAP polypeptide, wherein the nucleotide sequence is operably linked to a heterologous promoter and is further comprised within a vector. Appellant has seen nothing in the record that supports the rejection of claim 59 as either anticipated or obvious over Nobori *et al.* The limitations of the claim are not present in the cited reference and not specifically addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 59, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

6. Claim 60 is separately patentable.

Claim 60 recites a nucleotide sequence encoding an MTAP polypeptide, wherein the nucleotide sequence is operably linked to a heterologous promoter and wherein the nucleic acid is comprised within a host cell. Appellant has seen nothing in the record that supports the rejection of claim 60 as either anticipated or obvious over Nobori *et al.* The limitations of the claim are not to be found within the cited reference and are not specifically addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 60, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is

requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

7. Claim 61 and its dependents are not anticipated, not obvious, and separately patentable.

Claim 61 recites an isolated nucleic acid segment of between about 21 and about 500 nucleotides in length that comprises a contiguous sequence from SEQ ID NO:1, or that specifically hybridizes to said contiguous sequence from SEQ ID NO:1 under stringent hybridization conditions. For the reasons advanced above, claim 61 is neither anticipated nor obvious in view of Nobori *et al.* In sum, Nobori *et al.* does not disclose any sequence of SEQ ID NO: 1 expressly or inherently. There is no basis in the record for the assertion that any nucleotide sequence disclosed by Nobori *et al.* has any relevant sequence similarity to SEQ ID NO: 1. Nor is there any basis in the record for a reasonable expectation of success in making and using such a sequence.

The limitations of claim 61 include limitations on the length of the isolated nucleic acid segment, *i.e.* of between 21 and about 500 nucleotides in length, which confer a scope separate from the remaining claims. Further, there is no limitation that the nucleic acid segment encode any particular polypeptide. Rather, the nucleic acid segment comprises a contiguous sequence from SEQ ID NO: 1 or one that specifically hybridizes to a contiguous sequence from SEQ ID NO: 1. The limitations of claim 61 provide separate grounds for patentability. In brief, even if claims to nucleic acid segments encoding a MTAP polypeptide were to be found invalid, which the Appellants contend would not be proper in any case, claim 61, drawn to nucleic acid segments that do not necessarily encode such polypeptides, but which are nevertheless selected

from SEQ ID NO: 1, would still be patentable. Claim 61 and its dependents are therefore separately patentable.

8. As dependents of novel and non-obvious claim 61, claims 62-66 are also not obvious, and separately patentable.

Claims 62-66 each depend from novel and non-obvious claim 61. As explained in above, a rejection to dependent claims 62-66 is overcome once an rejection to independent claim 61 is overcome. Claims 62-66 are therefore separately patentable.

9. Claim 67 and its dependents are not anticipated, not obvious, and separately patentable.

Claim 67 recites a vector comprising at least a first nucleotide sequence that encodes a mammalian methylthioadenosine phosphorylase polypeptide comprising the amino acid sequence of SEQ ID NO:2. Claim 67 and its dependents are rejected solely on the grounds that they are anticipated by the disclosure of Kamb *et al.* As argued above, the disclosure of Kamb *et al.* does not anticipate the present claims. Indeed, the limitations of claim 67 recite that the nucleotide sequence encode the MTAP polypeptide of SEQ ID NO: 2 and Kamb does not disclose either expressly or inherently any polypeptide sequence of SEQ ID NO: 2, let alone the sequence in its entirety. No other grounds for rejection have been asserted against these claims. Therefore, even if the balance of the claims were held unpatentable, which they are not, on the basis of the record these claims are separately patentable over the remaining claims.

10. As dependents of novel and non-obvious claim 67, claims 68 and 69 are also not obvious, and separately patentable.

Claims 68 and 69 incorporate the limitations of claim 67, from which they depend, but each further contains limitations that make them narrower in scope. Claim 68 includes the

limitation that the nucleotide sequence comprises the nucleic acid sequence of SEQ ID NO: 1. Therefore, even if claim 67 is found unpatentable, which it is not, claim 68, including the novel and non-obvious limitation that the nucleic acid sequence comprise SEQ ID NO: 1 would remain patentable.

Similarly, claim 69 further includes the limitation that the vector of claim 67 be incorporated within a cell. Therefore, even if claim 67 is found unpatentable, which it is not, claim 69, including the novel and non-obvious limitation that the vector be comprised within a cell would remain patentable.

11. Claim 70 and its dependents are not anticipated, not obvious, and separately patentable.

Claim 70 recites a host cell comprising at least a first nucleotide sequence that encodes a mammalian methylthioadenosine phosphorylase polypeptide comprising the amino acid sequence of SEQ ID NO:2. Claim 70 and its dependents are rejected solely on the grounds that they are anticipated by the disclosure of Kamb *et al.* As argued above, the disclosure of Kamb *et al.* does not anticipate the present claims. Indeed, the limitations of claim 70 recite that the polypeptide comprise the sequence of SEQ ID NO: 2 and Kamb does not disclose either expressly or inherently any polypeptide sequence of SEQ ID NO: 2, let alone the sequence in its entirety. No other grounds for rejection have been asserted against these claims. Therefore, even if the balance of the claims were held unpatentable, which they are not, on the basis of the record these claims are separately patentable over the remaining claims.

12. Claim 71 is separately patentable.

Claim 71 depends from claim 70, further specifying that the nucleotide sequence comprises the nucleic acid sequence of from about nucleotide 122 to nucleotide 970 of SEQ ID NO: 1. Claim 71 is solely rejected as anticipated by the disclosure of Kamb *et al.*, which, as argued above, does not disclose either the amino acid sequence of SEQ ID NO: 2 nor the nucleic acid sequence of from about nucleotide 122 to nucleotide 970 of SEQ ID NO: 1. Nevertheless, if claim 70 were found to be unpatentable, *i.e.* that Kamb *et al.* disclose the amino acid sequence of SEQ ID NO: 2, which Appellant contends is not the case, Kamb *et al.* still fails to disclose any part of SEQ ID NO: 1. Claim 71 therefore would be separately patentable from the balance of the claims.

13. Claims 72 and 73 are each independently and separately patentable.

Claim 72 depends from claim 70, further specifying that the host cell is a prokaryotic cell. Similarly, claim 73 further specifies that the host cell is a eukaryotic cell. Appellant has seen nothing in the record that supports the rejection of either claim 72 or 73 as anticipated by Kamb *et al.*. Whether the host cell is prokaryotic or eukaryotic is nowhere addressed in rejecting these claims.

If the Examiner is not convinced of the independent patentability of each of claims 72 and 73, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

14. Claim 77 is separately patentable because a method of making a MTAP polypeptide is novel and not obvious.

Claim 77 recites a method of making a MTAP polypeptide. Appellant has seen nothing in the record that supports the rejection of claim 77 as obvious over Nobori *et al.* The limitations of the claim are not provided by or suggested anywhere in the Nobori *et al.* reference. Claim 77 is therefore not obvious in view of Nobori *et al.*, and since claim 77 is rejected solely over Nobori *et al.* under 35 U.S.C. §103(a), claim 77 is separately patentable from the balance of the claims.

If the Examiner is not convinced of the independent patentability of claim 77, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

15. Claim 78 and its dependents are not anticipated, not obvious, and separately patentable.

Claim 78 recites a method of detecting a nucleic acid segment comprising a sequence region encoding a MTAP polypeptide. The limitations of claim 78 provide separate grounds for patentability. Claims 79-83, incorporating the patentable limitations of claim 78 are therefore also separately patentable. A proper rejection under 35 U.S.C. §103(a) requires that the Examiner establish that the elements missing from the broader claim but present in the narrower claim are taught in the art. The Action asserts that the presently claimed methods are anticipated or rendered obvious by Nobori *et al.* or anticipated by Kamb *et al.* As argued above, neither reference anticipates or renders obvious the detection of nucleic acids encoding MTAP. Therefore, even if the broader claims were unpatentable, which they are not, on the basis of the

record claim 78 is not obvious nor anticipated. Therefore, claim 78 should stand or fall separately.

16. Claim 79 is separately patentable.

Claim 79 recites the method of claim 78 wherein the sample nucleic acids contacted are located within a cell, *i.e.* in situ hybridization. Appellant has seen nothing in the record that supports the rejection of claim 79 as either anticipated or obvious over Nobori *et al.* The limitations of the claim are not to be found within the cited reference and are not specifically addressed by the arguments advanced in rejection.

If the Examiner is not convinced of the independent patentability of claim 60, even in light of these compelling arguments, and intends to rely upon common knowledge in the art or well known prior art to assert the obviousness of the limitations of the claim, the Examiner is requested to support such assertion by citation to a reference or by an Examiner's affidavit pursuant to MPEP 2144.03.

H. Entry of The Amendment Will Put the Claims in Better Condition for Appeal

Provided the Amendment After Final submitted under 37 C.F.R. §1.116 is admitted, dependent claim 91 more clearly claims the present invention by correctly specifying that claim 91 depends from claim 90. Entry of the amendment will therefore put claim 91 in better condition for appeal.

Appellant has also submitted an amendment to correct a typographical error in the preliminary amendment of August 19, 1999, which incorrectly recited the filing date of

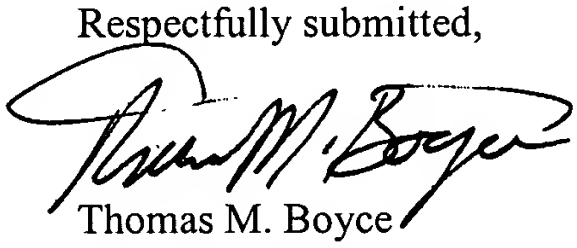
application serial number 60/000,831 as July 2, 1995. The correct filing date of application serial number 60/000,831 is July 3, 1995. Entry of the amendment will therefore put all claims in better condition for appeal, since the amendment corrects a date of priority of which the application claims the benefit.

Conclusion

Appellant has provided arguments that overcome the pending rejections. Appellant respectfully submits that the rejections asserted in the Final Office Action are unwarranted or improper. It is therefore requested that the Board overturn the rejections.

Please date stamp and return the enclosed postcard to evidence receipt of this document.

Respectfully submitted,



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